REMARKS

These remarks are in response to the Office Action mailed July 3, 2007. Claim 31 has been cancelled without prejudice to Applicant's right to prosecute the cancelled subject matter in a divisional, continuation, continuation-in-part, or other application. Claims 15-16, 22-24 and 32 have been amended. The amendments incorporate subject matter from claims 23 and 32, currently under examination, and thus do not raise issues requiring a further search. No new matter is believed to have been introduced.

I. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 15-18, 21-26 and 29-34 stand rejected under 35 U.S. C. §112, first paragraph, because while the specification is enabling for a method for administration of a neurotensin agonist to a subject with reduced pre-pulse inhibition, thereby promoting an elevation in the PPI response inhibition, the specification allegedly does not enable a method of modulating sensorimotor gating in a subject having a neuropsychiatric disorder, such as bipolar disorder, by administering any neurotensin agonist, thereby increasing PPI. Claim 31 has been cancelled, thus the rejection is moot with respect to this claim. Applicant respectfully traverses this rejection with respect to the amended claims.

Prepulse inhibition is a type of sensorimotor gating recognized in the art (see, e.g., Hedley *et al.* cited by the Examiner). Sensorimotor gating disorders in subjects with neuropsychiatric disorders are often measured by prepulse inhibition measurements. The Office Action, mailed October 2006, alleges at paragraph 21:

> . . .although an induce[d] deficit in PPI in adult rats may have a valid relationship to key psychophysiologic impairments related to schizophrenia["] and bipolar disorder, ["] it might bear no relationship to the pathogenesis of the disorder. . . .

Thus, Applicant submits that the rat model having induced PPI deficit are recognized models of schizophrenia as recognized in the art (including Hedley *et al.*) and by the Examiner. Furthermore, as the specification demonstrates DOI is an agonist of the serotonin-2 receptors not dopamine receptors. Blocking of the serotonin-2 receptor produces therapeutic benefit for a wide variety of psychiatric disorders other than

schizophrenia. The specification and data show that neurotensin agonists such as NT69L and PD149163 reverse the effects of DOI, For example, PPI disruption produced by DOI demonstrates that this class of compounds also block transmission at the serotonin 2A receptor. This was not known to be a pharmacological property of neurotensin agonists prior to the present invention studies.

The animal model of PPI disruption produced by drugs such as amphetamine or DOI provides information about the pharmacological properties of drugs that can reverse such disruption. A drug which reverse PPI disruption by amphetamine, a dopamine receptor agonist, may not reverse PPI disruption by DOI which is a serotonin-2 agonist and vice versa. Regardless of pathophysiology relationship, drug-induced PPI disruption provide a specific *in vivo* "assay" to obtain knowledge about the specific pharmacological properties of a test drug. This function of the drug induced PPI disruption rat model was the relevant feature underlying the discovery of new, therapeutically relevant, pharmacological properties associated with neurotensin agonists such as NT69L and PD.

Applicant respectfully submit that the methods of treatment described and claimed are not seeking to identify the origin (i.e., the pathogenesis) of the disease, but treat a subject that has the disease, a symptom of which is decreased PPI (a symptom treated by the invention). As the Examiner correctly points out in the office actions, the PPI rat model has a valid relationship to key psychophysiological impairments including schizophrenia and bipolar disorders. Thus, Applicant's claimed invention bears a reasonable correlation to the disease to be treated as recognized by the Examiner and those of skill in the art.

Furthermore, for Hedley, *et al.*, (currently cited under §102), to be a proper §102 reference, the Examiner must consider the single paragraph of Hedley *et al.*, to be an enabling disclosure. Applicant submits that the Office Action alleges that the present application is non-enabling because PPI in the rat model "might bear no relationship to the pathogenesis of the disorder. . ." of schizophrenia disorders, bipolar disorder and the like, while simultaneously citing Hedley *et al.* as an enabling disclosure for the treatment of schizophrenia based upon PPI in the rat model. As mentioned above, the Hedley et al. rat model and the rat model used in the present

specification are pharmacological models having a correlation to symptomatic criteria of bipoloar, schizophrenia, anxiety and depression.

The present application comprises a thorough description of compositions, methods of administration, diseases, disorders, and animal models (59 pages, including drawing and claims) and is allegedly non-enabling, while a single abstract page, Hedley *et al.*, is an alleged enabling disclosure.

Applicant respectfully submits that if the Patent Office maintains that Hedley *et al.* is an enabling disclosure for purposes of §102, then clearly, Applicant's disclosure must also be enabling. For at least the foregoing reasons, Applicant respectfully requests withdrawal of the enablement rejection.

II. REJECTION UNDER 35 U.S.C. §102(b)

Claims 15-18, 22, 24-26 and 31 stand rejected under 102(a) as allegedly anticipated by Hedley *et al.* (Soc. For Neurosc. Meeting Abs., August 2002). Claim 31 has been cancelled, thus the rejection is moot with respect to this claim. Applicant respectfully traverses this rejection.

As demonstrated by the attached Affidavit by Dr. David Feifel, the cited reference is not prior to Applicant's invention date and thus is not available under 35 U.S.C. §102(a). The attached Affidavit by Dr. Feifel demonstrates conception and diligence until reduction to practice of the invention now claimed including the use of NT69L in various mental disorders including schizophrenia.

Furthermore, the attached reference, Shilling et al., provides additional evidence of the efforts of Dr. Feifel, prior to the publication of Hedley et al. In the reference the Examiner will note that the manuscript was sent for peer review on May 10, 2002 (prior to Hedley et al., publication). Applicant notes that the publication of Schilling et al. is after Applicant's priority date. Accordingly, the only rejection pending under §102 may be properly withdrawn.

For at least the foregoing reasons, Applicant submits that all rejections may be withdrawn and the claims are now in condition for allowance.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY LLP

Date: January 3, 2008

By: _____
Joseph R. Baker
Registration No. 40,900

P.O. Box 1404
Alexandria, VA 22313-1404
858.509.7300 (Voice)
858.509.7353 (Fax)